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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/921,947 | 08/03/2001 | Michel Andre Crepeau | PM 01038 (5500*86) | 8375 |

23416 7590 11/08/2002

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| EXAMINER | |
|---|---|
| WELLS, LAUREN Q | |
| ART UNIT | PAPER NUMBER |
| 1617 | |

DATE MAILED: 11/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/921,947 | Applicant(s) CREPEAU, MICHEL ANDRE | |
|---|---|---|---|
| | Examiner Lauren Q Wells | Art Unit 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

Claims 1-57 are pending. The Amendment filed 6/19/02, amended claims 1, 5, 13, 20, 23, 24, 31, 33, 42 and 42, and added claims 44-57.

### *Response to Applicant's Arguments/Amendment*

Applicant's arguments with respect to the rejections of claims 1-43 under 35 USC 103 and 112, first paragraph, have been considered but are moot in view of the new ground(s) of rejection. However, the Examiner has responded to the arguments to the extent that they may be relevant to the present rejection.

Applicant's amendment filed 6/19/02, Paper No. 6, is sufficient to overcome the 112, 2nd paragraph, rejections in the previous Office Action.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16, 18-36, 38-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising the precursor of vitamin A, retinyl propionate with or without vitamin D3, and /or the precursor of vitamin E, dl alpha tocopherol acetate with or without vitamin D3 (see specification, pg. 3, lines 16-21, p. 7-8, Table 1, especially "Precursor", p. 10-14, Examples 1-5), does not reasonable provide enablement for any 2 or more precursors of vitamin A with or without vitamin D3, and/or any 2 or more precursors or vitamin E with or without vitamin D3. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

1. Nature of the invention. The instant invention pertains to a composition comprising one or more precursors of vitamin A and/or one or more precursors of vitamin E and/or vitamin D3, a C4-C6 alkyl lactate, one or more veterinarily acceptable emulsifiers, water, and oil

2. The state of the prior art. The skilled artisan would view vitamins to be a diverse group of compounds which encompass numerous organic chemicals, the precursors of which may constitute carbon, any of a number of pro-vitamins which are metabolized in vivo to the vitamin, and all intervening compounds.

3. The predictability or lack thereof in the art: It is a well-settled fact that metabolism of pro-drugs or pro-vitamins are often not predictable. It is well known that enzyme systems to metabolize pro-drugs or pro-vitamins differ between animal species, and that efficacy or toxicity often cannot be accurately predicted for one species, given the administration of the compound to another. It is also well known that a single atom addition or omission to any compound often results in the compound having an unpredictable biological activity. Because a compound necessarily needs the metabolic conversion from the pro-drug or pro-vitamin to the drug or vitamin in order to be considered a precursor thereof, and since the metabolism of any compound is unpredictable between species, undue experimentation would be required in order to further identify "precursors" of vitamins A and E useful in the compositions herein.

4. The amount of direction or guidance present: The specification provides one example of a vitamin A precursor, one example of a vitamin E precursor, and speculative inclusion of

optionally substituted oily derivatives of the vitamins (see specification, p. 3, lines 16-21, p. 7-8, Table 1, especially "precursor", p. 10-14, Examples 1-5).

5. The presence or absence of working examples: Seventeen examples of compositions employing the vitamin A precursor, retinyl propionate, alone, as a vitamin precursor are given (see pg. 9, line 1-p. 11, line 11). A single example of a composition employing the vitamin E precursor, dl alpha tocopherol acetate, alone, as a vitamin precursor is given (see p. 11, line 14-p. 12, line 14). A single example of a composition employing vitamin D3, alone, is given (see p. 12, line 15-p. 13, line 11). A single example of a composition employing the vitamin A precursor, retinyl propionate, the vitamin E precursor, dl alpha tocopherol, and vitamin D3 is given (see p. 13, line 15-p. 14, line 15).

Therefore, since the art of metabolic conversion is highly unpredictable, little direction and guidance was provided in the specification, and very limited examples of what may be considered precursors to vitamins A and E, undue experimentation would be required to practice the claimed invention.

***NOTE***: This rejection can be overcome by deleting the term "one or more" when it refers to precursors of Vitamin A and E, in the pending claims.

***Response to Applicant's Arguments***

Applicant argues, "In the present situation, an artisan can choose from the precursors of Vitamin A and Vitamin E that are known at the time he wishes to prepare a liquid vitamin composition according to the claims and combine them in amounts that fall within the range specified in the present claims". This argument is not persuasive. The Examiner respectfully points out that Applicant has provided no showings that Vitamin A and Vitamin E precursors are

well known in the art. The Examiner respectfully points out that showings of fact are much preferred to statements of opinion. In re Oelrich, 198 USPQ 210, 215 (CCPA 1978).

Applicant argues, "it is incorrect to say that the artisan is not enabled by the teachings of the present application simply because certain precursors may be incompatible with the other components of the composition nor may fail to form the desired vitamins in-vivo". This argument is not persuasive. The Examiner respectfully points out that it would be impossible for one of ordinary skill in the art to test every single possible precursor of vitamin A, every single possible precursor of vitamin E, and combinations thereof. The number of possible precursors is innumberable.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-9, 11-16, 18-27, 29, 31-36, 38-41, 44-45, 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over MVI-12 package insert in view of Lundberg.

MVI-12 package insert discloses a water-dispersible, substantially non-combustible and substantially flammable-alcohol/mono-hydroxy alcohol free liquid vitamin composition comprising 1mg retinol (vitamin A precursor), 10mg dl-alpha tocopheryl acetate (vitamin E precursor), 1.6% polysorbate 80 (emulsifier), water, 30% propylene glycol (stabilizer), BHT and BHA (antioxidants), gentisic acid ethanolamide (antifungal preservative). See entire disclosure. The reference lacks C4-C6 alkyl lactate and preferred percent weights.

Lundberg discloses sec-butyl lactate, isobutyl lactate, and n-butyl lactate as known solvents for oils. Alkyl lactates are disclosed as non-ozone-depleting and biodegradable solvents. Specifically, n-butyl lactate is disclosed as slightly soluble in water, miscible in alcohol and ether, and with many lacquer solvents, diluents, and oils.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the alkyl lactates of Lundberg to the composition of MVI-12 because of the expectation of further solubilizing the lipophilic constituents of MVI-12 and of providing an environmentally friendly composition.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the percent weights of MVI-12 as that of the instant invention, since it has been held that discovering an optimum value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

Claims 17, 37, 42, 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over MVI-12 in view of Lundberg as applied to claims 1-9, 11-16, 18-27, 29, 31-36, 38-41, 44-45, 49-51 above, and further in view of Multi-12 package insert.

MVI-12 and Lundberg are applied as discussed above. The reference lacks vitamin D3.

Multi-12 package insert discloses a water-dispersible, substantially non-combustible and substantially flammable-alcohol/mono-hydroxy alcohol free liquid vitamin composition comprising vitamin A palmitate (vitamin A precursor oil), dl-alpha tocopheryl acetate (vitamin E precursor), vitamin D3, polysorbate 80 (emulsifier), and water. See page 1.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the vitamin D3 of Mult-12 to the composition of MVI-12 because a) MVI-12

and Multi-12 are both directed to multi-vitamin compositions for intravenous infusion; b) MVI-12 and Multi-12 both teach ascorbic acid, vitamin A, thiamine, niacinamide, tocopheryl acetate, folic acid, biotin, cyanocobalamin, polysorbate 80, and sodium hydroxide as constituents of their compositions; c) Multi-12 additionally teaches vitamin D3 as a constituent of their composition and further teaches vitamin D3 as soluble in polysorbate 80, which is a solvent in MVI-12, and; e) MVI-12 teaches vitamin D as a constituent of its composition and vitamin D3 is an animal derived form of vitamin D. Thus, one of skill in the art would have been motivated to add the Vitamin D3 of Multi-12 to the composition of MVI-12 because of the expectation of providing a multi-vitamin that in addition to providing the physiological benefits associated with vitamins C, A, D, B1, B2, B6, and E, also provides the physiological benefits associated with vitamin D3, such as good bone and teeth formation.

Claims 10, 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over MVI-12 in view of Lundberg as applied to claims 1-9, 11-27, 29, 31-45, 49-51 above, and further in view of The Merk Index.

MVI-12 and Lundberg are applied as discussed above. The references lack ethoxyquin.

The Merk Index discloses that ethoxyquin is a known antioxidant used in food (see p. 593, item 3710).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute ethoxyquin for the BHT and/or BHA in the combined references since it is considered prima facie obvious to substitute any known antioxidant, such as BHT or BHA, with another known antioxidant, absent evidence to the contrary.

Claims 46-48, 52-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over MVI-12 in view of Lundberg in further view of Multi-12 as applied to claims 1-9, 11-16, 18-27, 29, 31-36, 38-41, 44-45, 49-51 above, and further in view of Boussouira et al.

MVI-12, Lundberg, and Multi-12 are applied as discussed above. The references lack retinyl propionate.

Boussouira et al. teach retinol and retinyl propionate as combinable and interchangeable retinoids for use in bio-affecting composition. See Col. 3, line 60-Col. 8, line 39.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute retinyl propionate for the retinol of MVI-12 because Boussouria et al. teach them as equivalent retinoids.

***Response to Arguments***

Applicant argues, "the dates printed on the two package inserts are not sufficient to establish that these documents are actually prior art to the present application". This argument is not persuasive. The Examiner respectfully points out that the M.V.I-12 package insert was revised in November 2000 (see bottom right corner of publication) and the Multi-12 package insert was published on May 16, 2000. The Examiner does not understand why Applicant does not find these dates sufficient.

Applicant argues, "an artisan of ordinary skill would not be motivated to simply add Vitamin D3 to the composition of MVI-12 without some teaching or suggestion that the new composition would be stable and there would be some advantage to adding vitamin D3". This argument is not persuasive. First, the Examiner respectfully points out that the test for obviousness is not whether the features of one reference may be bodily incorporated into the

other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the art. In the instant case, MVI-12 and Multi-12 are both directed to multi-vitamin compositions for intravenous infusion. MVI-12 and Multi-12 both teach ascorbic acid, vitamin A, thiamine, niacinamide, tocopheryl acetate, folic acid, biotin, cyanocobalamin, polysorbate 80, and sodium hydroxide as constituents of their compositions. Multi-12 additional teaches vitamin D3 as a constituent of their composition and further teaches vitamin D3 as soluble in polysorbate 80, which is a solvent in MVI-12. Thus, one of skill in the art would have been motivated to add the Vitamin D3 of Multi-12 to the composition of MVI-12 because of the expectation of providing a multi-vitamin that in addition to providing the physiological benefits associated with vitamins C, A, D, B1, B2, B6, and E, also provides the physiological benefits associated with vitamin D3, such as good bone and teeth formation. Second, the Examiner respectfully points out that this argument is not commensurate in scope with independent claim 1, which does not require vitamin D3 as a constituent.

Applicant argues, "There is no teaching or suggestion in any of the cited references that it would be beneficial or advantageous to use a C4 to C6 alkyl lactate component in addition to other known solubilizers". This argument is not persuasive. The Examiner respectfully points out that Lundberg teaches lactate esters as solvents known for use in pharmaceuticals and additionally teaches them as non-ozone-depleting and biodegradable. Lundberg specifically teaches n-butyl lactate as slightly soluble in water, miscible in alcohol and ether, and with many lacquer solvents, diluents, and oils. Thus, one of skill in the art would have been motivated to add the alkyl lactates of Lundberg to the MVI-12 because of the expectation of further solubilizing the lipophilic constituents of MVI-12.

Applicant argues, "there is no explanation in the Office Action as to why this rejection is relevant to claims 20-39, 41, 43, 45, 48, 51, 54 and 57, which claim the use of a C1 to C3 alkyl lactate instead of a C4 to C6 alkyl lactate". This argument is not persuasive. First, the Examiner respectfully points out that the reference relied upon to teach alkyl lactates, Lundberg, teaches C1-C6 alkyl lactates as interchangeable solvents for use compositions. Second, the Examiner respectfully points out that C3 and C4 alkyl lactates are homologues and that adjacent homologs are considered to be obvious absent unexpected results. In re Henze, 85 USPQ 261, 263 (CCPA 1950).

Applicant argues, "This argument is a classic case of hindsight reconstruction. If the cited documents do not contain any teachings concerning the properties recited in the claims of the present application, why would an artisan modify the composition and amounts of the various components in order to achieve those properties". This argument is not persuasive. The Examiner respectfully points out that while the references do not teach the ranges recited in the instant invention, the references do disclose percent weights of the constituents in the composition that fall within the ranges recited in the instant claims.

Applicant argues, "In accordance with the Examiner's reasoning, this means that the compositions of the present claims contain at least 22% by weight of solubilizers. In contrast MVI-12 composition contains only 1.6% by weight of polysorbate 80". This argument is not persuasive. The Examiner respectfully points out that MVI-12 additionally teaches 30% propylene glycol and propylene glycol is defined as an emulsifier (see dictionary definition provided by Examiner).

***Note***

The Examiner respectfully points out that claim 28 appears to be missing.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is (703) 305-1878. The examiner can normally be reached on M-F (7-5:30), with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (703)305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

lqw
October 4, 2002

SREENI PADMANABHAN
PRIMARY EXAMINER

10/3/02